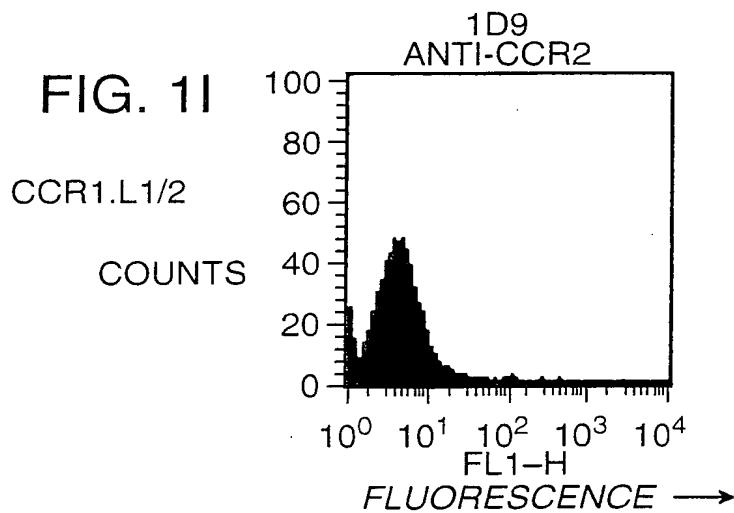
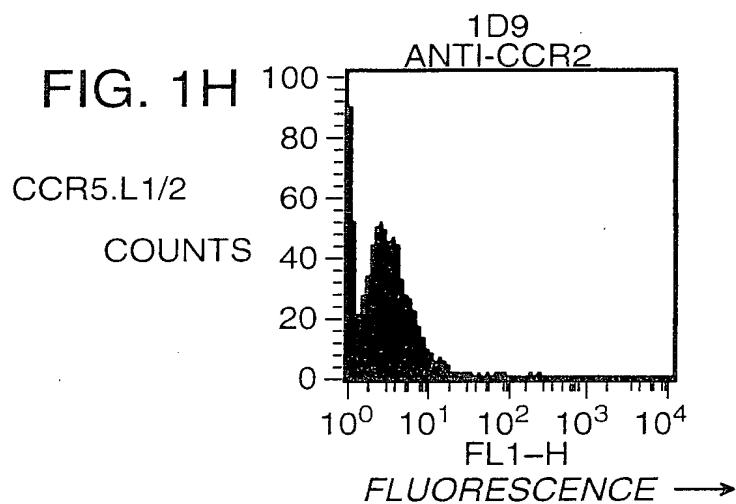
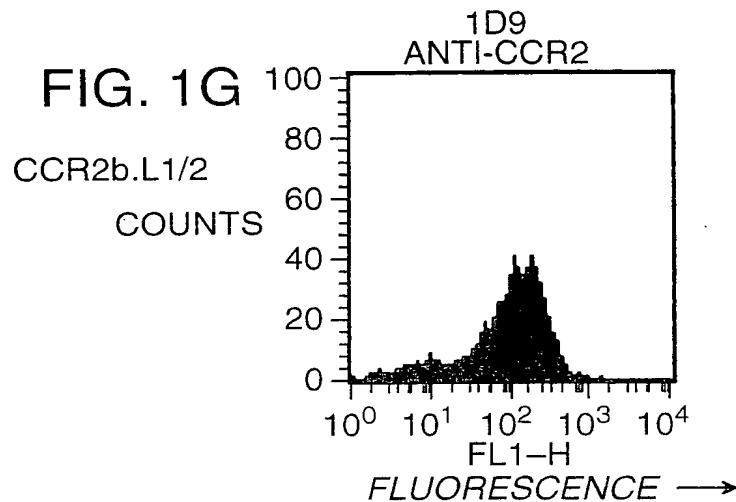
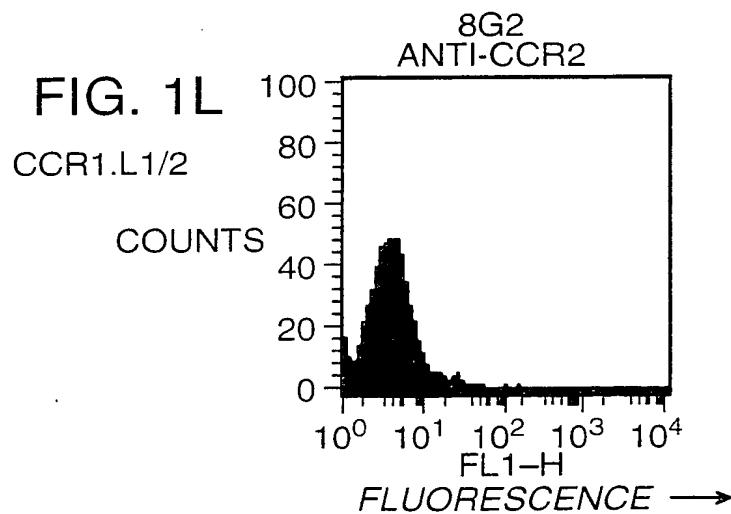
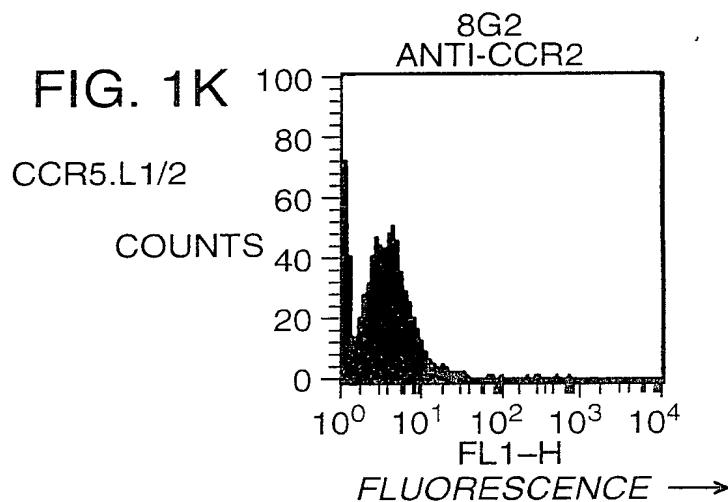
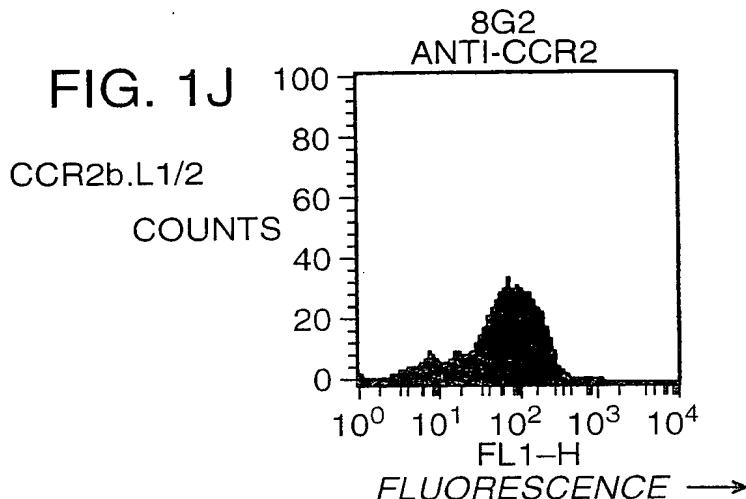


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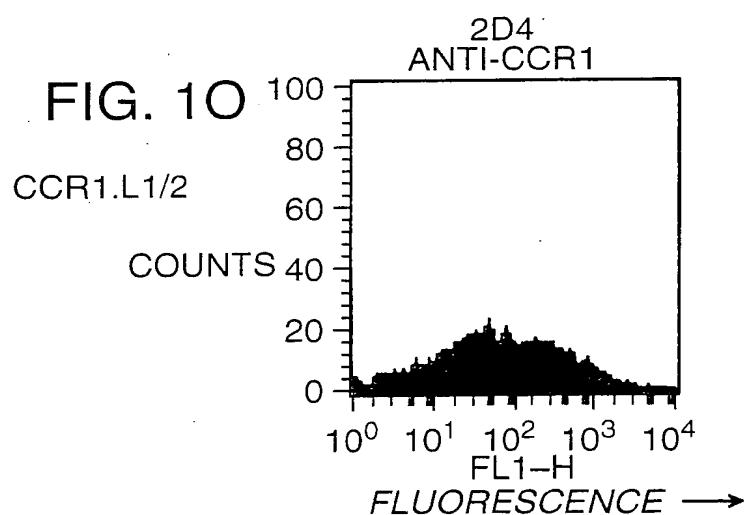
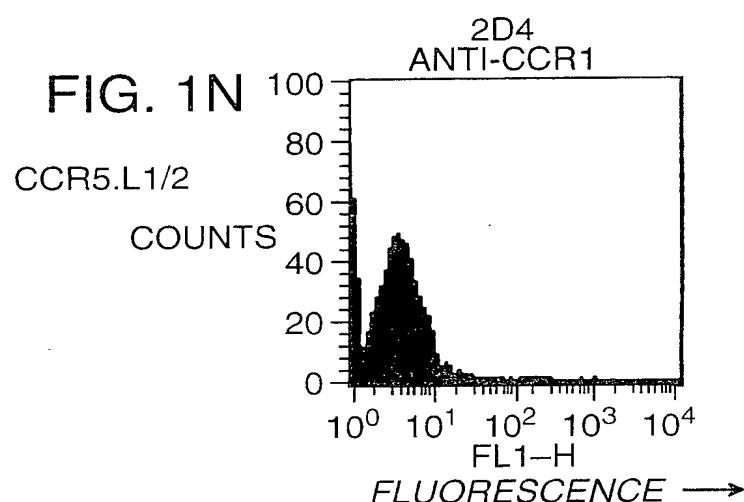
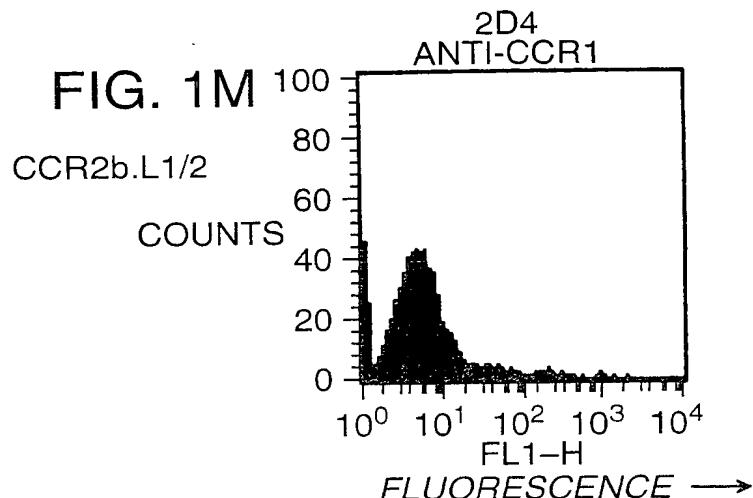
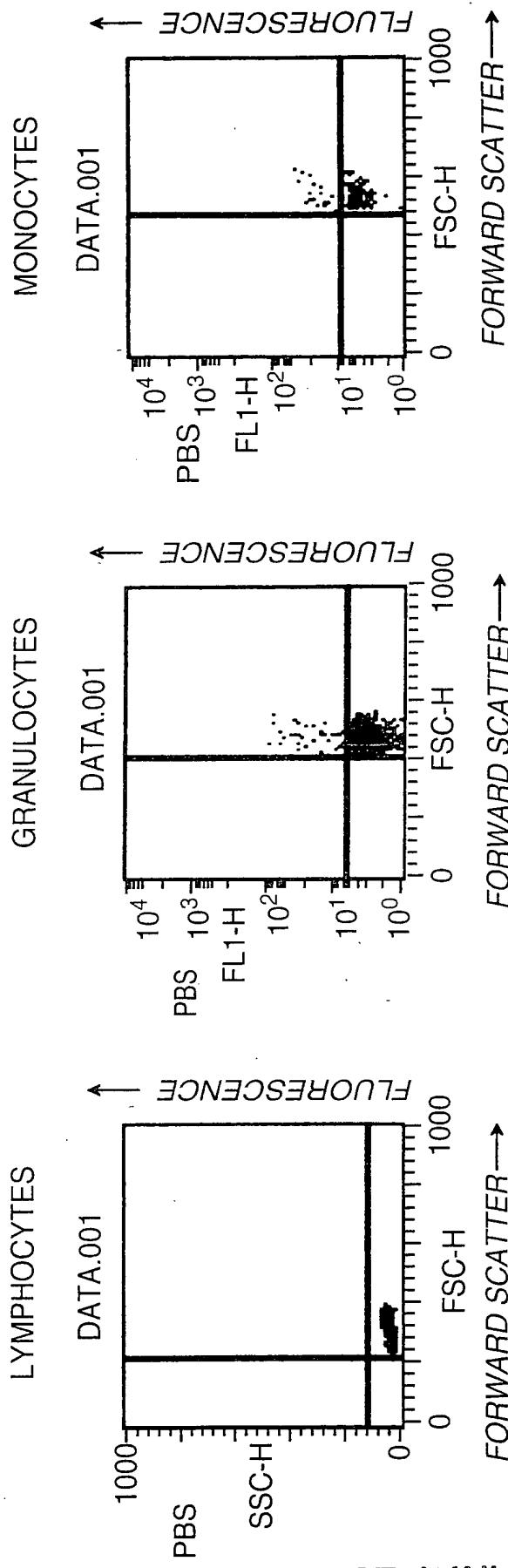


FIG. 2A
FIG. 2B
FIG. 2C



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FIG. 2D

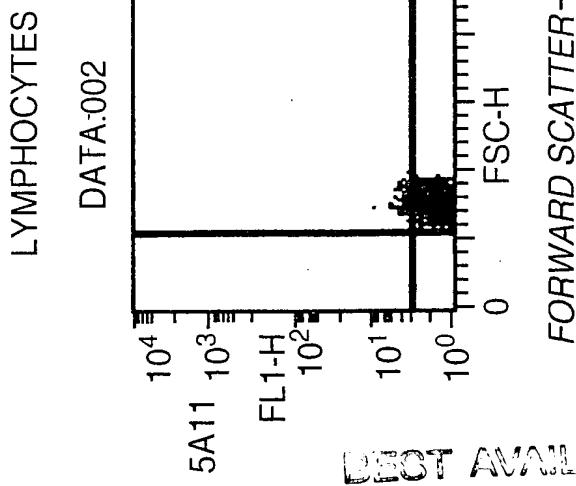


FIG. 2E

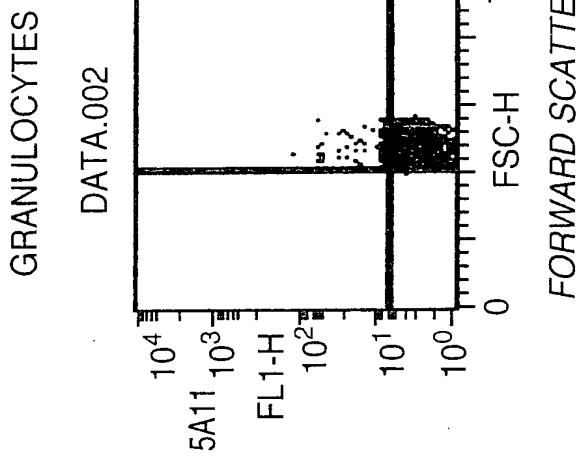


FIG. 2F

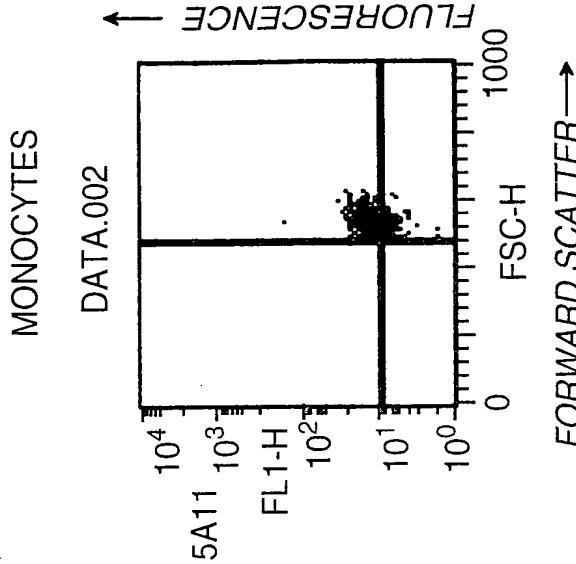


FIG. 2G
FIG. 2H
FIG. 2I

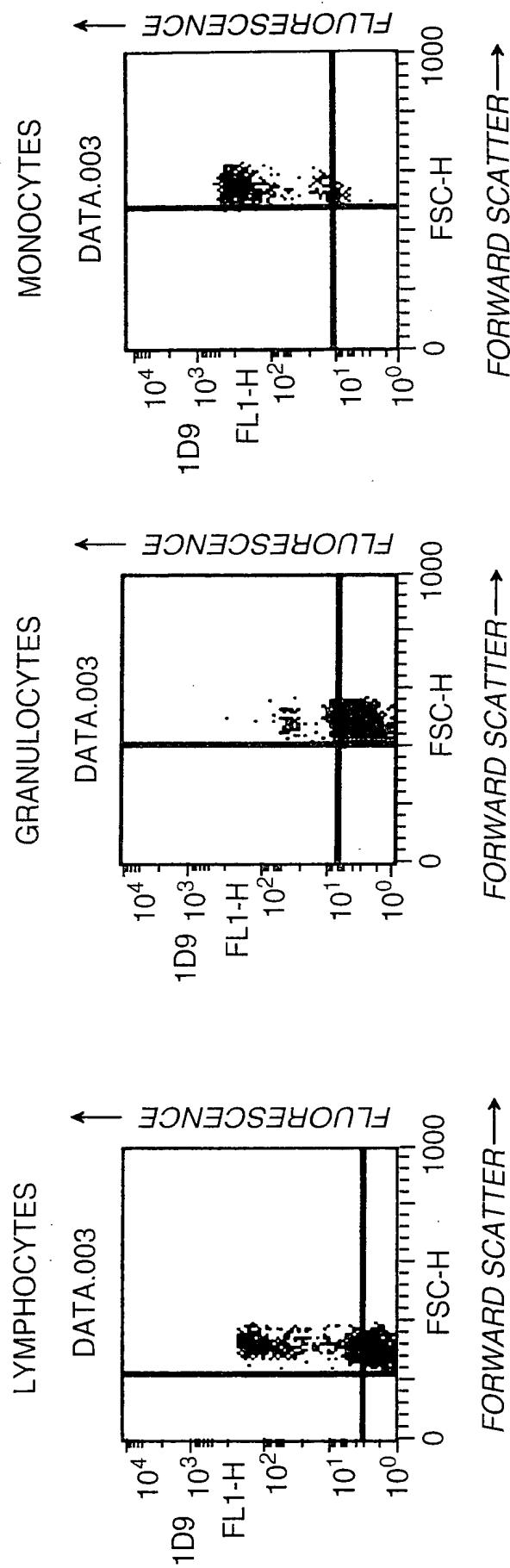


FIG. 2L

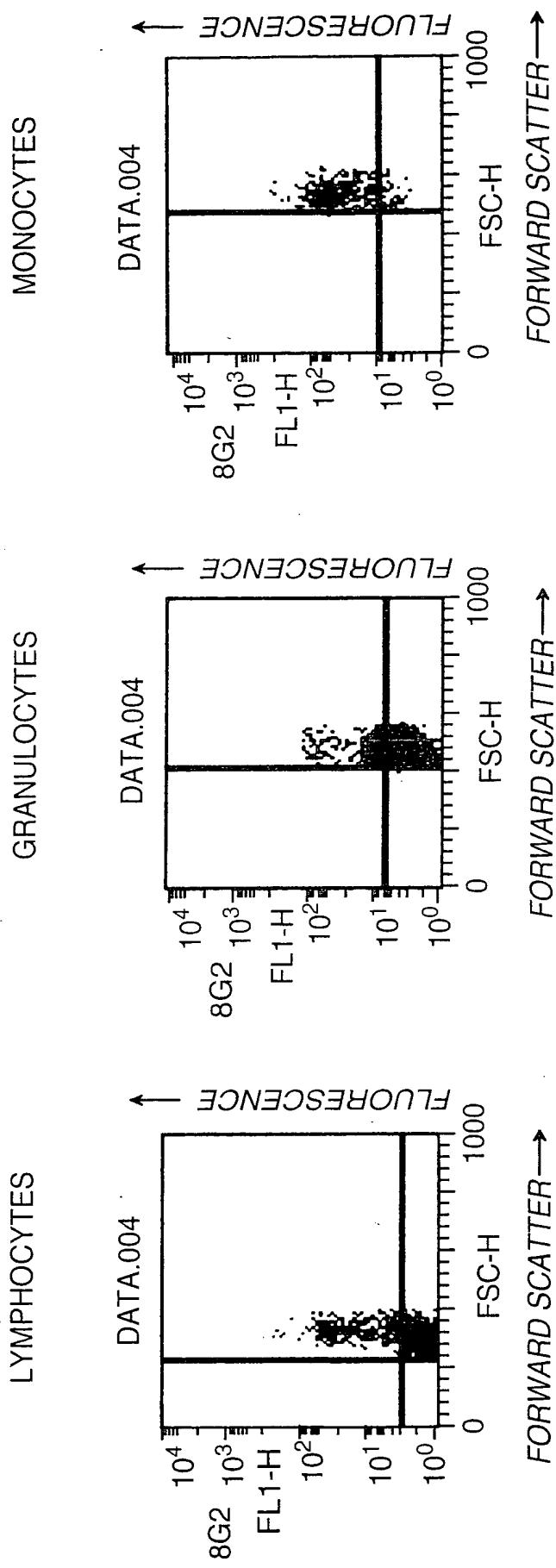


FIG. 2K

LYMPHOCYTES

FIG. 3A

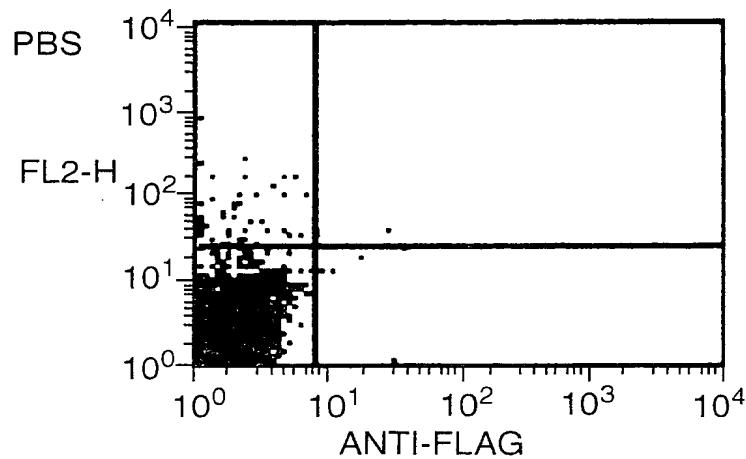


FIG. 3B

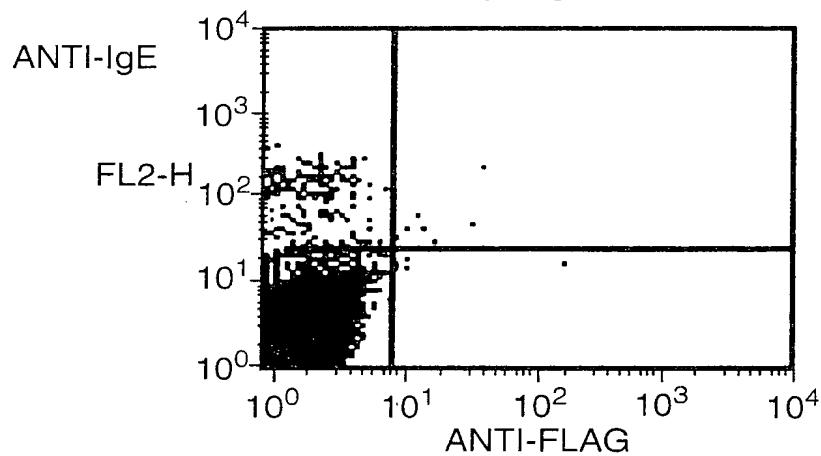
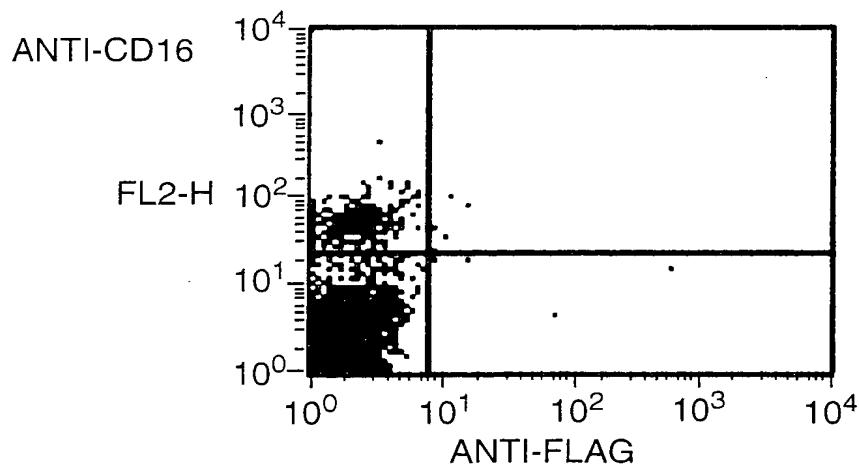


FIG. 3C



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FIG. 3D

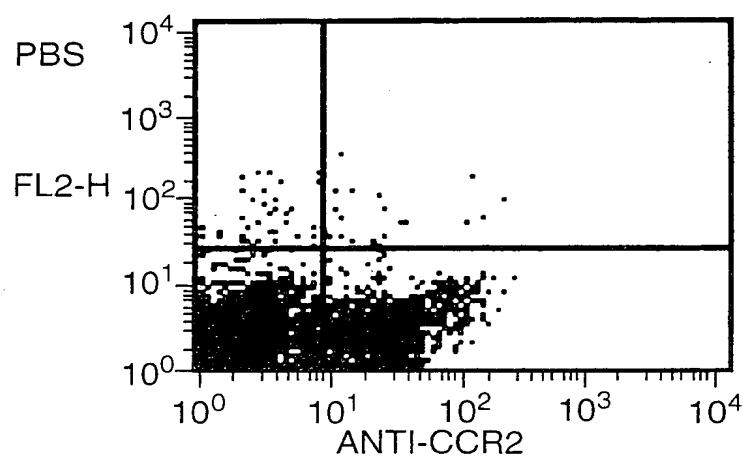


FIG. 3E

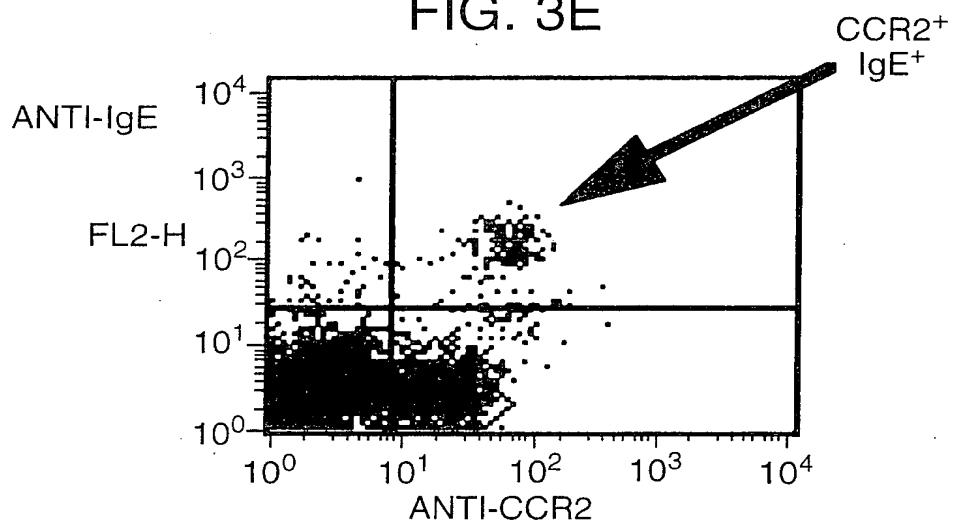


FIG. 3F

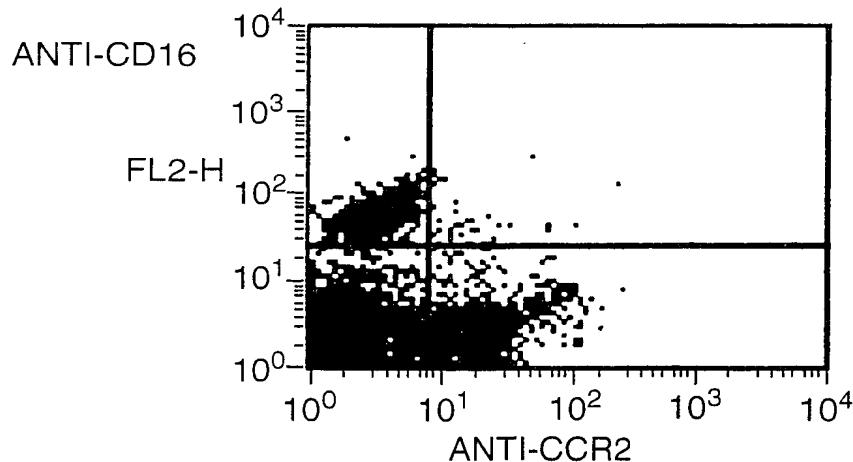


FIG. 3G

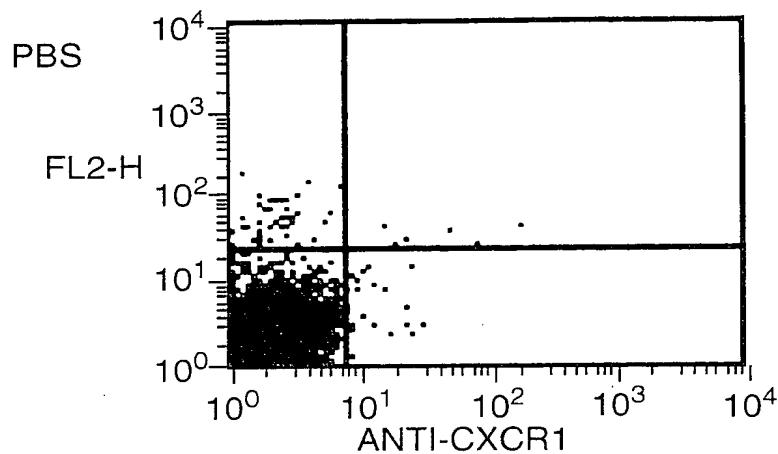


FIG. 3H

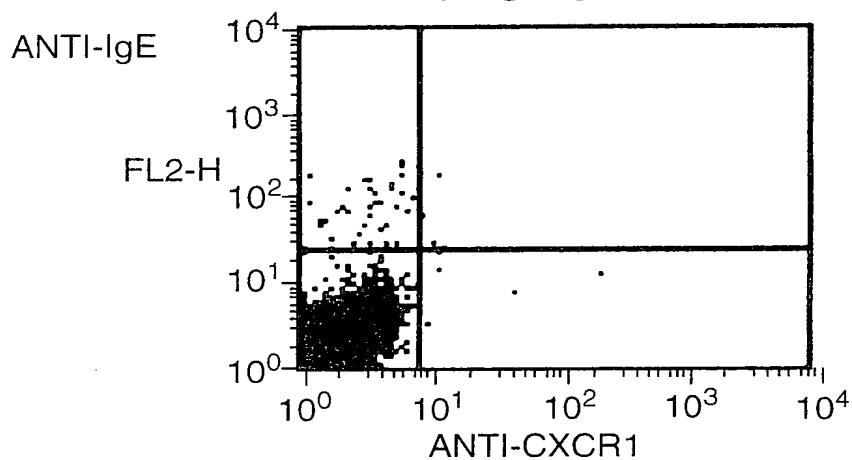
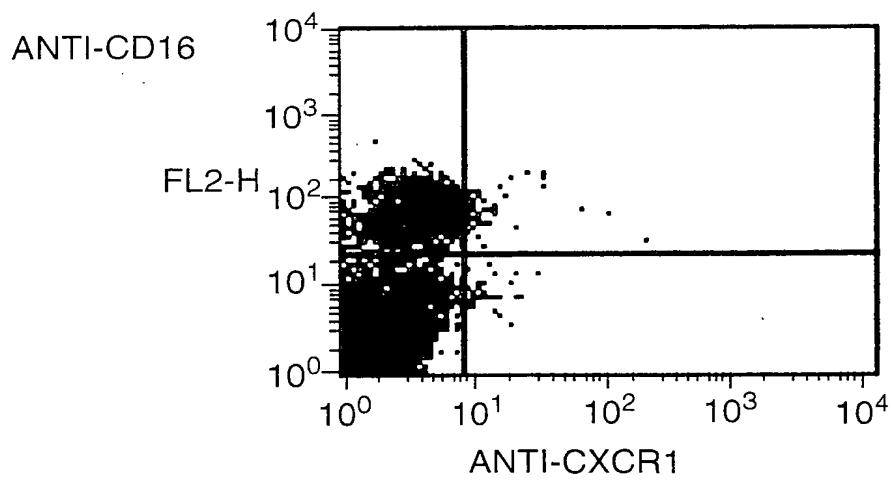


FIG. 3I



REJECT ANTI-CD16 CCR2

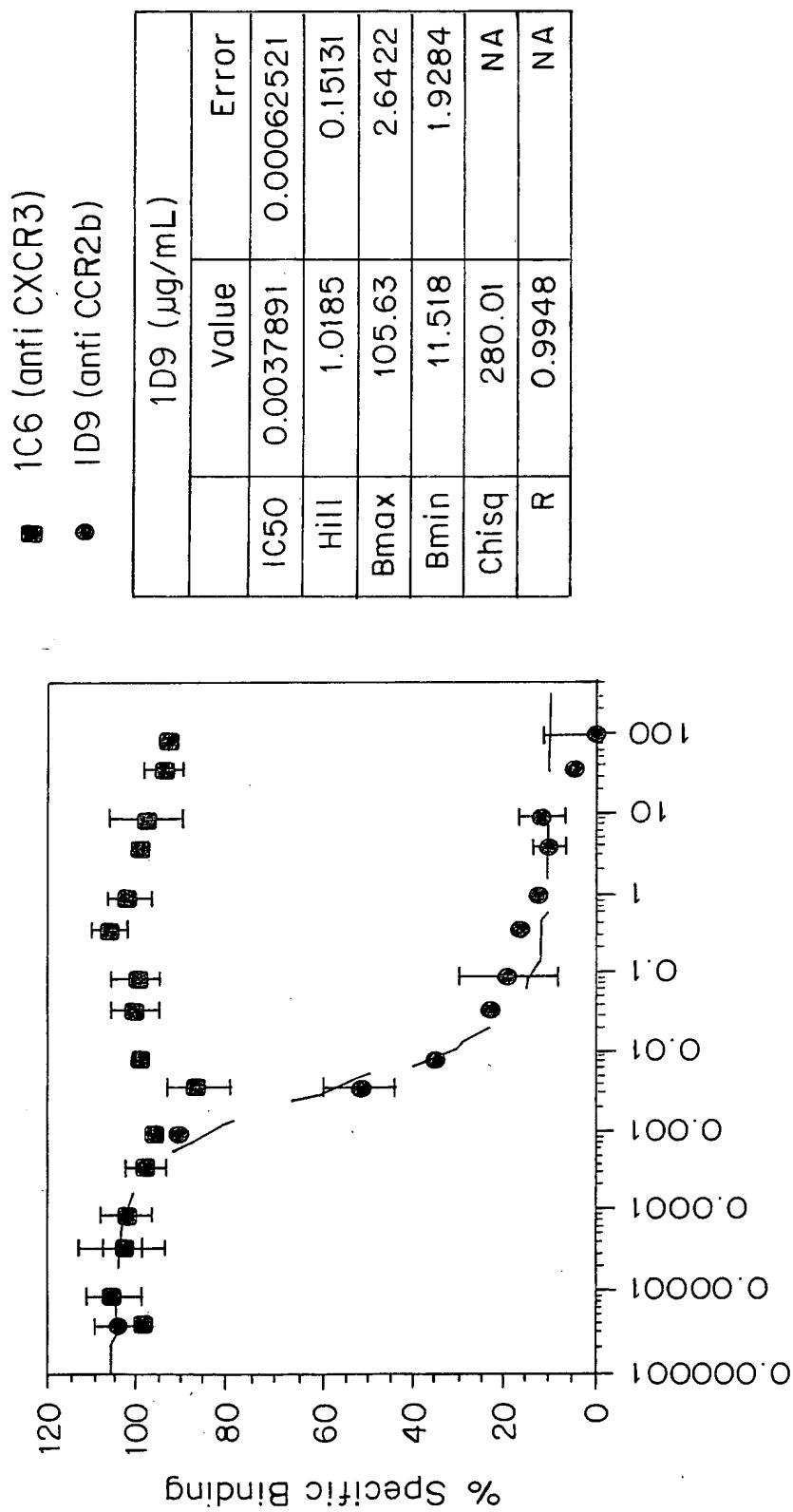


FIG. 4

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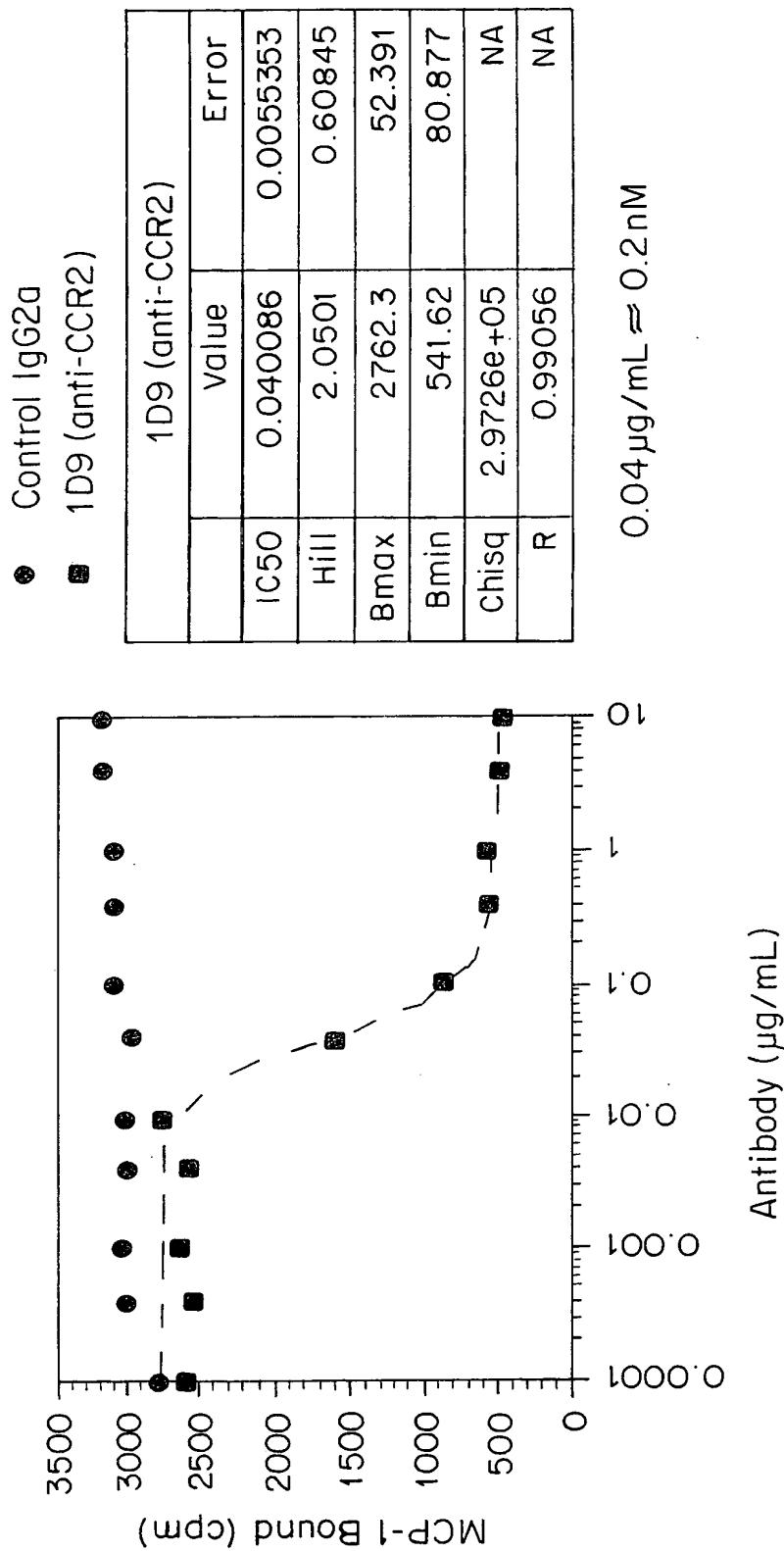


FIG. 5

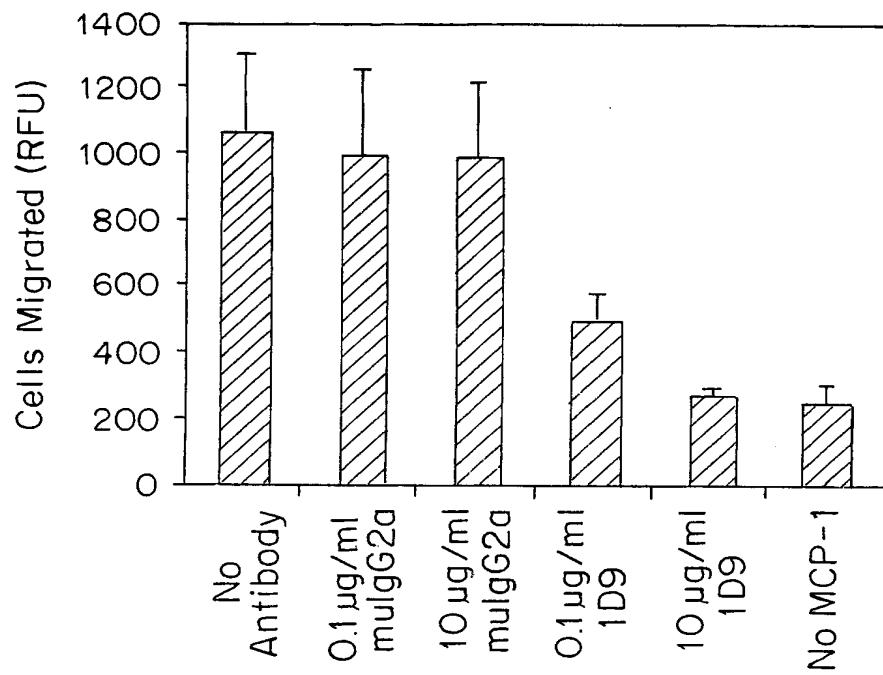


FIG. 6A

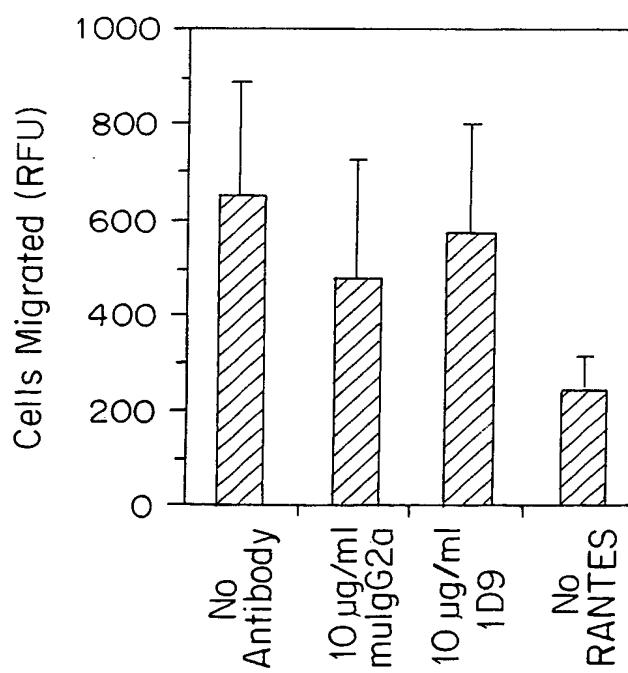


FIG. 6B

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

}

1 DVVMTQTPLT LSVTVGHPAS ISC**KSSQSLL** DSDGKT**F**LNW LLQRPGQSPK

51 RLIY**LVS**KLD SGVPDRFTGS GSGTDFTLKI SRVEAEDLGV YYC**WQGTHFP**

101 **YTF**GGGTKLE IK

Figure 7

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*]

1 EVQLVESGGG LVQPK GSLKL SCAAS GFSFN **AYAMN WVRQA PGKGLEWVAR**

51 **IRTKNNNYAT YYADSVKD** RY TISR DDSESM LFLQMNNLKT EDTAMYYCVT

101 **FYGNGVWGTG TT** TVSS

Figure 8

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

Chothia Canonical Classes

L1 (16 amino acids) = Class 4
Key residues: **2(V)**, 25(SA), 29(L), 33(L), **71(F)**

L2 (7 amino acids) = Class 1
Key residues: **48(IV)**, 51(AT), 52(ST), **64(G)**

L3 (9 amino acids) = Class 1
Key residues: 90(QNH), 95(P)

Martin Canonical Classes

L1 (16 amino acids) = Class 4/16A
Key residues: **2(V)**, **4(ML)**, **23(C)**, 25(SSP), 26(SN),
27(Q), 29(LI), 30A(HL), 30B(S),
30C(NDS), 30D(G), 32(YS), 33(LF),
34(HEN), **35(W)**, 51(V), **71(F)**, **88(C)**,
90(Q), 92(TS), 93(H)

L2 (7 amino acids) = Class 1/7A
Key residues: **23(C)**

L3 (9 amino acids) = Class 1/9A
Key residues: **2(IVL)**, **3(VQLE)**, **4(ML)**,
28(SNDTE), 30(DYLVISNFGHT),
31(SNTKG), 32(FYNAHSR),
33(MLVIF), **88(C)**, 89(QSGFL),
90(QNH), 91(NFGSRDHTYV),
92(NYWTSRQHAD),
93(ENGHTSRAQHAD),
94(DYTVLHNNIWPS), 95(P),
96(PLYRIWF), 97(T), **98(F)**

Figure 9

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.* }
}

Chothia Canonical Classes

H1 (5 amino acids) = Class 1
Key residues: **24(AVG), 26(G), 27(FY)**

H2 (19 amino acids) = Class 4
Key residues: **54(S), 55(Y), 71(R)**

Martin Canonical Classes

H1 (5 amino acids) = Class 1/10A
Key residues: **2(VIG), 4(LG), 20(LIMV), 22(C),
24(TAGVS), 26(G), 29(IFLS),
32(IHYFTNCED), 33(AWGTLV),
34(IVMW), 35(HENQSYT), 36(W),
48(IMLV), 51(LIVTSN),
69(ILFMV), 78(ALVYF), 80(LM),
90(YF), 92(C), 94(RKGSNH),
102(YHVISDG).**

H2 (19 amino acids) = Class ?/12B
Key residues: **47(W), 50(RQ), 51(I), 59(Y), 69(I),
71(R), 78(LV)**

Figure 10

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

CDRs

Key

1D9 V _k	Mouse 1D9 V _k region
HF-21/28 V _k	Chosen human framework acceptor V _k region sequence with mismatches to the 1D9 V _k region highlighted.
1D9RK _A V _k	CDR grafted 1D9 V _k region, with no back mutations but with the added human lysine residue at position 107 (i.e. 107K)
1D9RK _B V _k	CDR grafted 1D9 V _k region, with back mutations at F36L and Q37L, and the additional 107K insertion.
1D9RK _C V _k	CDR grafted 1D9 V _k region, with back mutations at F36L, Q37L and Q100G, and the additional 107K insertion.
1D9RK _D V _k	CDR grafted 1D9 V _k region, with back mutations at F36L, Q37L, Q100G and Q17H, and the additional 107K insertion.

Figure 11

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

Key

1D9 V _H	Mouse 1D9 V _H region.
4B4'CL V _H	Chosen human framework acceptor V _H region sequence with mismatches to the 1D9 V _H region.
1D9RH _A V _H	CDR grafted 1D9 V _H region, with no back mutations.
1D9RH _B V _H	CDR grafted 1D9 V _H region, with back mutations at T28S and S30N.
1D9RH _C V _H	CDR grafted 1D9 V _H region, with back mutations at T28S, S30N, G49A and F67Y.
1D9RH _D V _H	CDR grafted 1D9 V _H region, with back mutations at T28S, S30N, G49A, F67Y and T93V.

Figure 12

Sequence Name Identical Residues Amino Acid Sequence

1D9 V _k	114	BWVMTQTPLTLGVPASTICKSSQSSLDS-DGKTEFLNWILLQRPQQSPKRLLYLVSKLDGSVPDRETGSQSGTDFTLKISRVEAEDLGYYCWQGTTHFP
70/3	97I.Q.....Y.....
70/1	94I.Q.....Y. N. Y.....V.P.....Y.....S.....
70/2	82XLHS.....I.Q.....Y. N. Y.....V.P.....Y.....S.....
V-1B	76S. P. SL. DQ.....R.....VH. N. N. Y. Y. K.L. R. .NRF.....S.....
V-1C	75S. P. SL. DQ.....R.....IVH. N. N. Y. E. Y. K.L. K. .NRLL.....S.....
V-1A/K5.1/K5.1	75S. P. SL. DQ.....R.....VH. N. N. Y. H. Y. K.L. K. .NRF.....S.....
V-1C/V1A5/K1A5	74	...L.....S. P. SL. DQ.....R.....IVH. N. N. Y. E. Y. K.L. K. .NRF.....S.....
K18.1	73	.A.....S. P. SL. DQ.....R.....EN. N. N. Y. Y. K.QL. R. .NRF.....L. S.....
1F	71	...LL.....F. P. SL. DQ.....S.....VH. N. NYY. E. H. KS.LQL. E. .RH.S.....
24A	68	.I.....AAFSNP..L. TS.....R.. K.H. S. N. Y. Y. F. K.QL. YI. N. A.S.....
167/24	67	.I. I. .DE. SNP..S. ESV.....R.. K.YK.Y. F.QL. M. TRA.S. S.....
24B	66	.I.....AAFSNP..L. TS.....R.. K.H. N. I. Y. Y. Y. K.QL. QM. N. A.SS. S.....

Figure 13

Sequence Name Identical Residues Amino Acid Sequence

1D9 V _H	117	EVQLESGGGLVQPKGSILKLSCAAASGFSFNAYAMN--WVRQAPGKGLEVARIRTKNNNYATYYADSVVKDRYTISRDDSESMLFLQMNNLKTEDTAMYCVTF
MRL-REF24BG	86VWWRM.....T..T.....F.....Q..Y.....S..SS.....I-
V(H)22.1	70	..K.E.....G..M.....V.....T.SN.W.S ..S.E.....O..L.SD.....H..E.....G.F.....K.SVY.....RA.....GI.....TG-
V11/pFV19B4	66	..K.....G..R.....T..TD.Y.S ..P..A..LGF..N.A.G.T.E.SA...G.F.....N.Q.I.Y.....T.RA..S.T..AR-
Vh7183 (Vh69.1)	66	..K.....K.G.....T.SS.T.S ..S.E.R.....T.SS--GGSY ..P....G.F.....NAKNT.Y.....SS..S.....TR-
VH10-1.9	65	D.K.....K.G.....T.SS.T.S ..T.E.R.....T.SS--GGSY ..P....G.F.....NAKNT.Y.....SS..S.....TR-
VHE4-ps1	65	.L..G..R.....T.SS...S ..T.E.R.....A.S.--DGSEI.XP.T..G.F.....NAKNT.....SS.RY.....LR-
V(H)50.1	65	..K.....G.....T..SD.Y.Y ..T.E.R.....Y.SN--GGGS ..P.T..G.F.....NAKNT.Y.....SS..S.....AR-
V3	65	..K.....GA..R.....S..T.TD.Y..HRP...P..L.L..N.A.G.I.E.SA.M.G.F.....N.Q.I.Y.....T.S..S.T..ARD
V1/pBV132	64	..K.....G..R.....T..T.SDFY.E ..P..R..I.AS.N.A.D.T.E.SA...G.FIV...T.Q.I.Y.....A.RA.....I..AR-
VH283	64	..M.....K.G.....T.SS.T.S ..T.E.R.....T.SS--GGGN ..P..G.F.....NAKNN.Y.....SS.RS.....L..AR-
V(H)37.1	63	..K.....K.G.....T..T.SS.G.S ..T.E.R.....T.SG--GGSY ..P....G.F.....NAKNN.Y.....SS.RS.....L..AR-
V13	61	..K.M.....GA..R.....E..T.TD.Y.'S ..L.R.SP..L.L..N.A.G.T.E.SA...G.F.....N.QNI.Y.....T.RA.A.S.T..AKD
V-H 441/V441	59	..K.L.....G.....D.SR.W.S ..IGE.NP--DSSTIN.TP.L..KFI.....NAKNT.Y.....SKVRS.....L..AR-
68-5N	59G.....T.SS.G.S ..T.D.R..L..T.NS--GGS ..P....G.F.....NAKNT.Y.....SS..S.....AR-
76-1BG/VH7183.9	58K.G.....T.SS...S ..T.E.R.....T.SS--GGSY ..P....G.F.....NAKNT.Y.....SS.RS.....AR-
61-1P	58G..R.....T.SSFG.H ..E.....Y.SS--GSSTI..T..G.F.....NPKNT.....TS.RS.....AR-
57-1M/VH7183.12	58K.G.....T.SS...S ..T.E.R.....S.S--SGGS ..P....G.F.....NARNI.Y.....SS.RS.....AR-
V(H)55	56	..K.L.....G..N.....D.SR.W.S ..A.....Q..IGE.NP--GSSTIN.TP.L..KFI.....NAKNT.Y.....SKVRS.....L..AR-
VH7183.13	55K.G.....T.SS.T.S ..T.E.R.....Y.SN--GGGS ..P.T..G.F.....NAKNT.Y.....SS..S.....AR-

Figure 14

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, et al.

Figure 15

Name	ID	Surface CDR	Core CDR	Kabat FR	FR Surface	Core FR	Vernier FR	V _k Near CDR	J Chain	Closest Human Germline Gene	L1 Class	LenL3 Class	L3 Class
1D9 V _k	100.0	30	82	32	82	22	60	33	14	100	14	16	7
036521	90.4	27	76	28	75	19	56	31	13	90	13	DPK19-A1+	Same
II.66	78.8	25	67	22	69	18	52	30	13	80	12	DPK18-A17+	Same
RPMI6410	78.8	25	67	22	69	18	52	30	13	79	12	DPK18-A17+	Same
ZM1-1	78.8	25	66	21	68	18	52	30	13	79	12	DPK18-A17+	Same
VL clone 54	78.1	25	66	21	68	18	52	30	13	79	12	DPK18-A17+	Same
HF-21/28	79.3	24	66	21	68	18	52	30	13	78	12	DPK18-A17+	Same
SpA2-08	77.9	24	65	21	68	18	51	30	13	77	12	DPK18-A17+	Same
II.30	77.9	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same
HUNVK	77.9	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same
O-81	75.7	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same
ToP309	74.8	24	64	20	68	18	51	29	12	76	12	DPK12-A2+	Same
ToP218	74.8	24	64	20	68	18	51	29	12	76	12	DPK12-A2+	Same
SpA3-02	76.1	24	63	20	68	18	51	29	12	76	12	DPK18-A17+	Same
II.37	75.2	24	63	20	68	18	51	29	12	76	12	DPK18-A17+	Same
CUM	73.9	24	63	20	68	18	50	29	12	75	12	DPK36-Chr22 4	17
VL clone 51	74.6	24	62	20	67	18	50	29	12	75	12	DPK18-A17+	Same
II.20	75.2	23	62	20	67	18	50	29	12	75	12	DPK18-A17+	Same

Figure 16

Figure 17A

Amino Acid Sequence

Figure 17B

Name	ID	All	Surface	Core	Kabat	FR	Core	FR	Vernier	V _H	J Chain	Closest Human	H1	H2	H3	H1	H2
					CDR	Surface	FR	Near				Germline Gene	Size	Size	Size	Class	Class
								CDR									
1D9 V _H	100.0	117	29	84	30	87	21	65	30	16	100	17	5	19	6	1	4
030094	67.7	86	19	67	15	72	17	57	26	12	75	13	DP-29-122+	Same	Same	16	Same
N51P8	68.3	86	18	66	15	72	16	57	25	12	75	13	DP-29-122+	Same	Same	15	? Same
IW2-91	67.5	85	18	65	15	72	16	56	25	12	75	12	DP-29-122+	Same	Same	15	Same
H2-46	66.7	84	18	65	15	72	16	56	25	12	75	12	DP-29-122+	Same	Same	15	Same
039158	72.2	83	17	64	15	71	15	56	25	12	74	12	DP-29-122+				
038064	65.6	82	17	64	14	71	15	56	25	11	74	12	VH26Rabbits+				
038062	64.6	82	17	63	14	71	15	56	25	11	73	12	VH26Rabbits+				
32.B9	64.6	82	17	63	14	71	15	56	25	11	72	12	VH26Rabbits+				
038062	64.6	82	17	63	14	71	15	56	25	11	72	12	VH26Rabbits+				
034514	69.8	81	17	63	14	70	15	56	25	11	72	12	VH26Rabbits+				
038066	65.3	81	16	63	14	70	15	55	25	11	71	12	VH26Rabbits+				
035365	65.9	81	16	63	14	70	15	55	25	11	71	12	VH26Rabbits+				

Figure 18A

Name	ID	All	Surface	Core	Kabat	FR	FR	Core	FR	Vernier	V _H	J Chain	Closest Human	Size	H1	H2	H3	Size	H1	H2	H3	Size	Class	Class	
					CDR	Surface	FR	Near	CDR				Germline Gene												
Hb-5	69.2	81	16	63	14	69	15	55	25	11	71	12	VH26Rabbits+		Same	17	16	Same	3						
4G12	64.8	81	16	63	14	69	15	55	25	11	71	12	VH26Rabbits+		Same	17	11	Same	3						
VH clone	66.7	80	16	63	14	69	14	55	25	11	71	12	VH26Rabbits+		Same	17	11	Same	3						
39	040094	62.5	80	16	63	14	69	14	55	25	11	71	12	LSG3.1		Same	17	18	Same	3					
VH clone	63.0	80	16	63	13	69	14	55	25	11	71	12	VH26Rabbits+		Same	17	18	Same	3						
18																									
UB1-24	67.2	80	16	63	13	69	14	55	25	11	71	12	DP-31-V39P+		Same	17	10	Same	3						
029764	64.5	80	16	63	13	69	14	55	25	11	71	12	VH26Rabbits+		Same	17	15	Same	3						
IW2-105	64.5	80	16	63	13	69	14	55	25	11	71	12	LSG3.1		Same	Same	13	Same	?						
UB1-17	65.0	80	16	63	13	69	14	55	25	11	71	11	LSG3.1		Same	Same	12	Same	?						
VH clone	66.1	80	16	62	13	69	14	55	25	11	71	11	VH26Rabbits+		Same	17	12	Same	3						
41	4B4'CL	67.2	80	16	62	13	68	14	55	25	11	71	11	LSG3.1		Same	Same	8	Same	?					
M26	65.0	80	16	62	13	68	14	55	25	11	71	11	LSG3.1		Same	Same	12	Same	?						

Figure 18B

Docket No.: 1855.1052-029
 Title: Humanized Anti-CCR2 Antibodies...
 Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _K	Mouse κ-II	Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core	1D9 RK _A	1D9 RK _B	Comment
1	1	FR1	D	D*	D		S	D	D	
2	2		V	V	I*		C	V	V	
3	3		V	V	V*		S	V	V	
4	4		M	M	M		C	M	M	
5	5		T	T*	T		C	T	T	
6	6		Q	Q*	Q		C	Q	Q	
7	7		T	T	S	S	S	S	S	
8	8		P	P	P		c	P	P	
9	9		L	L	L		s	L	L	
10	10		T	S	S	S	C	S	S	
11	11		L	L	L*		c	L	L	
12	12		S	P	P	P	c	P	P	
13	13		V	V*	V*		c	V	V	
14	14		T	S	T		c	T	T	
15	15		V	L	P	L	s	L	L	
16	16		G	G	G		c	G	G	
17	17		H	D	E	Q	c	Q	Q	
18	18		P	Q	P		s	P	P	
19	19		A	A	A		c	A	A	
20	20		S	S*	S		c	S	S	
21	21		I	I*	I		c	I	I	
22	22		S	S*	S*		C	S	S	
23	23	FR1	C	C	C		C	C	C	
24	24	CDR1	K	R	R	R	s	K	K	
25	25		S	S*	S*		c	S	S	
26	26		S	S*	S		s	S	S	
27	27		Q	Q	Q		s	Q	Q	
27A	28		S	S	S		s	S	S	
27B	29		L	L	L		c	L	L	
27C	30		L	V	L	V	s	L	L	
27D	31		D	H	H	H	c	D	D	
27E	32		S	S	S		s	S	S	
27F	33		-	x				-	-	
28	33		D	N	D		s	D	D	
29	34		G	G*	G		c	G	G	
30	35		K	N	N	N	c	K	K	
31	36		T	T	N		c	T	T	
32	37		F	Y*	Y	Y	c	F	F	
33	38		L	L*	L		c	L	L	
34	39	CDR1	N	E	N		c	N	N	
35	40	FR2	W	W	W		C	W	W	
36	41		L	Y	Y	F	C	F	L	Δ1

Figure 19A

Kabat	#	FR or CDR	Mouse 1D9 V _K	Mouse κ-II		Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK _A	1D9 RK _B	Comment
37	42		L	L		L	Q	c		Q	L	Δ2
38	43		Q	Q*		Q		c		Q	Q	
39	44		R	K		K		c		R	R	
40	45		P	P*		P		s		P	P	
41	46		G	G*		G		s		G	G	
42	47		Q	Q		Q		c		Q	Q	
43	48		S	S*		S		c		S	S	
44	49		P	P*		P		C		P	P	
45	50		K	K		Q	R	c		R	R	
46	51		R	L		L		C		R	R	
47	52		L	L*		L		C		L	L	
48	53		I	I*		I		C		I	I	
49	54	FR2	Y	Y		Y		C		Y	Y	
50	55	CDR2	L	K		L		c		L	L	
51	56		V	V		V	K	c		V	V	
52	57		S	S		S		c		S	S	
53	58		K	N		N		c		K	K	
54	59		L	R		R	N	c		L	L	
55	60		D	F		A	R	c		D	D	
56	61	CDR2	S	S*		S		s		S	S	
57	62	FR3	G	G		G		S		G	G	
58	63		V	V		V		C		V	V	
59	64		P	P		P		C		P	P	
60	65		D	D*		D		S		D	D	
61	66		R	R		R		C		R	R	
62	67		F	F*		F		C		F	F	
63	68		T	S		S	S	C		S	S	
64	69		G	G*		G		C		G	G	
65	70		S	S*		S		C		S	S	
66	71		G	G*		G		C		G	G	
67	72		S	S*		S		s		S	S	
68	73		G	G*		G		C		G	G	
69	74		T	T*		T		C		T	T	
70	75		D	D*		D		C		D	D	
71	76		F	F*		F		C		F	F	
72	77		T	T*		T		c		T	T	
73	78		L	L		L		c		L	L	
74	79		K	K		K		c		K	K	
75	80		I	I		I		c		I	I	
76	81		S	S		S		c		S	S	
77	82		R	R*		R		s		R	R	
78	83		V	V		V		c		V	V	
79	84		E	E		E		s		E	E	
80	85		A	A*		A		c		A	A	
81	86		E	E*		E		s		E	E	
82	87		D	D*		D		c		D	D	
83	88		L	L		V	V	c		V	V	
84	89		G	G*		G		c		G	G	
85	90		V	V		V		c		V	V	
86	91		Y	Y*		Y		c		Y	Y	
87	92		Y	Y		Y		C		Y	Y	
88	93	FR3	C	C		C		C		C	C	

Figure 19B

Docket No.: 1855.1052-029
 Title: Humanized Anti-CCR2 Antibodies...
 Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _K	Mouse κ-II		Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK _A	1D9 RK _B	Comment
89	94	CDR3	W	F		M		c		W	W	
90	95		Q	Q*		Q	M	c		Q	Q	
91	96		G	G		A		c		G	G	
92	97		T	T		L		c		T	T	
93	98		H	H		Q		c		H	H	
94	99		F	V		x		s		F	F	
95	100		P	P*		P	W	c		P	P	
95A			-	P		R				-	-	
95B			-	-		-				-	-	
95C			-	-		-				-	-	
95D			-	-		-				-	-	
95E			-	-		-				-	-	
95F			-	-		-				-	-	
96	101		Y	Y		x	-	c		Y	Y	
97	102	CDR3	T	T*		T	F	c		T	T	
98	103	FR4	F	F*		F		C		F	F	
99	104		G	G		G		c		G	G	
100	105		G	G		Q	Q	c		Q	G	
101	100		G	G		G		c		G	G	
102	106		T	T		T		c		T	T	
103	107		K	K*		K	R	s		R	R	
104	108		L	L		V		c		L	L	
105	109		E	E		E		s		E	E	
106	110		I	I		I		s		I	I	
106A			-	-		-				-	-	
107	111	FR4	K	K*		K	-	s		K	K	

Figure 19C

Kabat	#	FR or CDR	Mouse 1D9 V _H	Mouse IIIc	Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core		1D9 RH _A	1D9 RH _B	Comment
1	1	FR1	E	E*	E		s		E	E	
2	2		V	V	V		C		V	V	
3	3		Q	K*	Q		s		Q	Q	
4	4		L	L*	L*		C		L	L	
5	5		V	E	V		s		V	V	
6	6		E	E	E		c		E	E	
7	7		S	S	S*		c		S	S	
8	8		G	G	G*		c		G	G	
9	9		G	G	G*		c		G	G	
10	10		G	G*	G		c		G	G	
11	11		L	L	L		S		L	L	
12	12		V	V*	V		c		V	V	
13	13		Q	Q	Q	K	s		K	K	
14	14		P	P	P*		c		P	P	
15	15		K	G	G*	G	s		G	G	
16	16		G	G	G		s		G	G	
17	17		S	S	S*		c		S	S	
18	18		L	M*	L*		c		L	L	
19	19		K	K*	R	R	c		R	R	
20	20		L	L	L		c		L	L	
21	21		S	S	S*		c		S	S	
22	22		C	C	C*		C		C	C	
23	23		A	V	A		c		A	A	
24	24		A	A	A		C		A	A	
25	25		S	S	S*		c		S	S	
26	26		G	G	G		c		G	G	
27	27		F	F	F*		C		F	F	
28	28		S	T*	T	T	C		T	S	Δ1
29	29		F	F*	F		C		F	F	
30	30	FR1	N	S	S	S	S		S	N	Δ2
31	31	CDR1	A	N	S	N	c		A	A	
32	32		Y	Y	Y	A	S		Y	Y	
33	33		A	T	A	W	S		A	A	
34	34		M	M	M		c		M	M	
35	35		N	N	S	S	c		N	N	
35a			-	-	-		c		-	-	
35b		CDR1	-	-	-		c		-	-	

Figure 20A

Kabat	#	FR or CDR	Mouse 1D9 V _H	Mouse IIc	Human III	Human Acceptor 4B4'CL (000490)	Surf ace Or Core		1D9 RH _A	1D9 RH _B	Comment
36	36	FR2	W	W	W*		C		W	W	
37	37		V	V	V*		C		V	V	
38	38		R	R	R*		C		R	R	
39	39		Q	Q	Q*		c		Q	Q	
40	40		A	S	A		c		A	A	
41	41		P	P	P		s		P	P	
42	42		G	E	G*		s		G	G	
43	43		K	K	K		s		K	K	
44	44		G	G	G		c		G	G	
45	45		L	L	L*		C		L	L	
46	46		E	E*	E		C		E	E	
47	47		W	W	W*		C		W	W	
48	48		V	V*	V*		C		V	V	
49	49	FR2	A	A	S	G	C		<u>G</u>	<u>G</u>	
50	50	CDR2	R	E	V		c		R	R	
51	51		I	I	I		c		I	I	
52	52		R	R	S	K	s		R	R	
52a	53		T	L	G	S	s		T	T	
52b	54		K	K	K*		s		K	K	
52c	55		N	S	T	T	c		N	N	
53	56		N	H	D	D			N	N	
54	57		N	N	G	G			N	N	
55	58		Y	Y	G	G			Y	Y	
56	59		A	A	S	T	s		A	A	
57	60		T	T	T		c		T	T	
58	61		Y	H	Y	D	c		Y	Y	
59	62		Y	Y	Y		c		Y	Y	
60	63		A	A	A		c		A	A	
61	64		D	E	D	A	s		D	D	
62	65		S	S	S	P	s		S	S	
63	66		V	V	V*		c		V	V	
64	67		K	K	K		s		K	K	
65	68	CDR2	D	G	G*	G	s		D	D	
66	69	FR3	R	R	R*		C		R	R	
67	70		Y	F	F*	F	C		<u>F</u>	<u>F</u>	
68	71		T	T	T		C		T	T	
69	72		I	I*	I*		C		I	I	
70	73		S	S	S*		S		S	S	
71	74		R	R	R*		C		R	R	
72	75		D	D	D		c		D	D	
73	76		D	D	N		C		D	D	
74	77		S	S	S		s		S	S	
75	78		E	K	K	K	s		<u>K</u>	<u>K</u>	
76	79		S	S	N	N	s		<u>N</u>	<u>N</u>	
77	80		M	S	T	T	c		<u>T</u>	<u>T</u>	
78	81		L	V	L		C		L	L	
79	82		F	Y	Y	Y	c		<u>Y</u>	<u>Y</u>	
80	83		L	L	L*		c		L	L	

Figure 20B

Kabat	#	FR or CDR	Mouse 1D9 V _H	Mouse IIIc	Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core	1D9 RH _A	1D9 RH _B	Comment
81	84		Q	Q*	Q		c	Q	Q	
82	85		M	M	M*		C	M	M	
82a	86		N	N	N		s	N	N	
82b	87		N	N	S	S	s	S	S	
82c	88		L	L	L*		c	L	L	
83	89		K	R	R		s	K	K	
84	90		T	A	A		c	T	T	
85	91		E	E	E		s	E	E	
86	92		D	D	D		C	D	D	
87	93		T	T	T		c	T	T	
88	94		A	G	A*		c	A	A	
89	95		M	I	V	V	c	V	V	
90	96		Y	Y	Y*		c	Y	Y	
91	97		Y	Y	Y*		C	Y	Y	
92	98		C	C*	C*		C	C	C	
93	99		V	T	A	T	C	T	T	
94	100	FR3	T	T	R		C	T	T	
95	101	CDR3	F	G	G	D	c	F	F	
96	102		Y	F	R	S	c	Y	Y	
97	103		G	-	x	L	s	G	G	
98	104		N	-	G	P	c	N	N	
99			-	-	x	P	c	-	-	
100			-	-	S	H	c	-	-	
100 a			-	-	L		C	-	-	
100 b			-	-	S		C	-	-	
100 c			-	-	G			-	-	
100 d			-	-	x			-	-	
100 e			-	-	Y			-	-	
100 f			-	-	Y			-	-	
100 g			-	-	Y			-	-	
100 h			-	-	Y			-	-	
100 i			-	-	H			-	-	
100 j			-	-	Y			-	-	
100 k			-	F	F		C	-	-	
101	105		G	A	D	R	C	G	G	
102	106	CDR3	V	Y	Y		C	V	V	
103	107	FR4	W	W	W*		C	W	W	
104	108		G	G	G*		C	G	G	
105	109		T	Q	Q	Q	S	Q	Q	
106	110		G	G	G*		C	G	G	
107	111		T	T	T*		C	T	T	
108	112		T	L	L	L	C	L	L	
109	113		V	V	V*		C	V	V	
110	114		T	T	T*		C	T	T	
111	115		V	V*	V*			V	V	
112	116		S	S	S*			S	S	
113	117	FR4	S	S	S*			S	S	

Figure 20C

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ATGGACTTCGGGTTAAACTTGGTTCTTGTGTTCAAGGTGCAATTGGAGGTGCAGCTTGGTGA
TACCTGAAGCCCAATTGAAACAAAAGAACAAACAAAAAATAGTCCACACGTAACACTCCACGTC
leader variable
M D F G L N L V F F V V F Y Q G V H C T E V Q L V E S G G G L V Q P
AAGGGTCATTGAAACTCTCATGTCAGCTTGGAATTCAAGCTTCAAGCTACGCCATGA
TTCAGTAACTTGAGAGTACACGTCGGAGACCTAAGTCGAAGTTACGGATGCGGTACT
K G S L K L S C A A S G F S F N A Y A M N W V R Q A P G K G L E W V
TGCTCGGATAAGAACCTAAAATAAATTATGCCAACAATTATGCCGATTCAAGTGAAAGACAGAT
ACGAGCGTATTCTGAGATTAAAGCTTCAAGCTAACGGCTAACGGCTAACGGCTAACGG
A R I R T K N N Y A T Y Y A D S V K D R Y T I S R D D S E S M L
TTCTTGCAAATGAAACAACCTGAAACTGAGGACACAGCCATGTTATTACTGTGACCTTACGGTA
AAAGACGTTTACTTGTGAACCTTGTGACTTTGACTCTGTGCGGTACATAATGACA
F L Q M N N L K T E D T A M Y Y C V T F Y G N G V W G T T V T
TCTCCCTCAGCCAAAACAAACAGCCCCATCCGCTATCCCCCTGGT
AGAGGAGTCGGTTTGTGTCGGTAGGGAGATAGGGGACCA
variable constant
V S S A | K T T A P S V Y P L V

Figure 21

ATGAAGTITGCCCTGGCTTAGGCTTGTGGATTGGGAGACAATGGCGATGTTGATGACCCAGACTCCACTTTCGGTTACCGTTGGAC
 TACTTCAACGGGACAATCCGACAACACAGACCAAACTAACCTAAGCCCTCTGGCTACAAACACTACTGGGTCTGAGGTGAGTAAACAGCCAATGGCAACCTG 100

M K L P V R L L W I R E T I G D V V M T Q T P L T P L T S V T V G
 ACCCAGGCCCTCCATCTCTTGCAAGTCAAAGTCAGAGCTCAGTGTAGATAGTGTAGAAAGACATTTTGAAATTGTTGTTACAGAGGCCAGTCTCCAAA 150

TGGGTCGGAGGTAGAGAACGTTCAAGTCAGTCACTACCTTCTGGGAAATCTATCACTACCTTCTGTTAAAAACCTAACCAAACAAATGTCCTCGGICGGTCAGAGGTTT 200

H P A S I S C K S S Q S L L D S D G K T F L N W L L Q R P G Q S P K
 GCGCCTAAATCTATCTGGTGTCTAAACTGGACTCTGGAGTCCCCTGACAGGTTCACTGGCAGTGGATCAGGGACAGATTTCACACTGAAAATCAGCAGAGTG 250

C CGGGATTAGATAGACCACAGATTGACCTGAGACCTCAGGGACTGTCAGTCACTAGTCCAAAGTGACCTAGTCCCCTGCTAAAGTGTGACCTTTAGTGCTCTCAC 300

R L I Y L V S K L D S G V P D R F T G S G T D F T L K I S R V
 GAGGTGAGGGATTGGGAGTTTATTTGCTGGCAAGGTACACATTTCGGTACACGTTGGGGGGACCAAGCTGGAAATAAAACGGGTGATGCTG 350

C TCCGACTCTAAACCTCTAAATATAACGACCGTTCAIGTGTAAAGGCATGCAAGCTTGGTTGACCTTATTGGCCGACTACGAC 400

E A E D L G V Y C W O G T H F P Y T F G G G T K L E I K R | A D A
 CACCAACTGIAATCCATCTCCACCA 426
 GIGGTGACATAGGTAGAAGGGTGGT
 APTRVSIFFPP

Figure 22

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GAGGTGCAATTGGTGTAGCTTGAGGAGGATTGGTGAAGCCCTGGGGGTCAATTGAGACTCTCATGTGCAGCCTCTGGATTCACTTCAGTCAGCTACGCCA
CTCCACGTTAACCAACTCAGACCTCCCTTAACCACTTGGACCCCCAGTAACCTCTGAGAGTACCGTGGAGACCTAACGTTAAGTGAAAGTCACGGATGCGGT 10

E V O L V E S G G G L V K P G G S L R L S C A A S G F T F S A Y A
TGAACCTGGGTCGGCAGGCCTCAGGAAGGGTTGGAAATGGGTGGCTGGCCGCAATTAGAACATAAAAATTAATGAAACATATTATGCCGATTCACTGAA 20

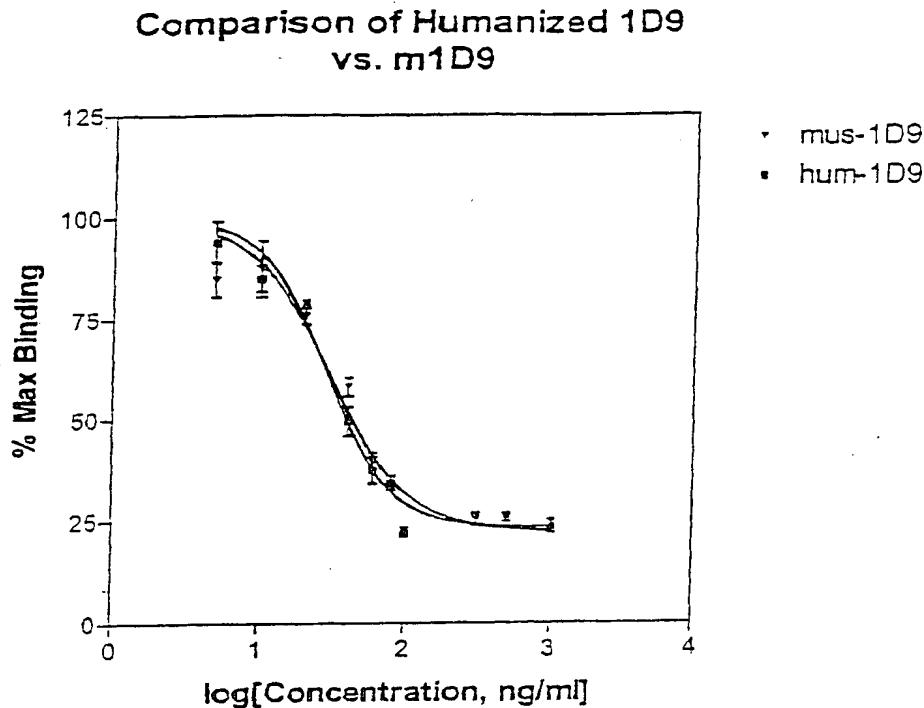
ACTTGACCCAGGGGTCGGGTCCTGGGTCCTTCCCACCCATTACCCAAACCTTACCTGCGTATTCTTGATTTTTAACTTAACTGTTGATAATACGGCTAAAGTCACCTT
M N W V R O A P G K G L E W V G R I R T K N N N Y A T Y Y A D S V K
AGACAGATTACCAATCACCAGAGATGATTCAAACACCCCTAATGAAACAGCTTGAAMACTGAGGACACAGCCGTTGAACTGTTGACCTGACCC 30

TCTGCTTAAGTGGTAGAGGTCTCTACTAAGTTTGTGGAGATAGACGTTTACTTGTCGAACCTTGTGACTTGTGTCGGCACATAATGACATGGTGG
D R F T I S R D D S K N T L Y L O M N S L K T E D T A V Y Y C T T
B₁P₁
TTTACGGTAACGGTGTGGGCAAGGGACCTGGTCACCGTCAGCTCAGCCAA 357
AAAATGCCATTGCCACAGACAGACCCCCGGTCCCCGGTGGGACCAAGTGGCAGTCGAGTCGGTTT
F Y G N G V W G Q G T L V T V S S A K

Figure 23

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Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

Figure 24



	hum-1D9	mus-1D9
Equation 1		
Best-fit values		
BOTTOM	23.46	22.40
TOP (Constant)	100.0	100.0
LOGEC50	1.452	1.472
HILLSLOPE	-1.972	-1.627
EC50	28.32	29.68
Std. Error		
BOTTOM	2.656	3.945
LOGEC50	0.04151	0.06251
HILLSLOPE	0.2946	0.3143
95% Confidence Intervals		
BOTTOM	17.18 to 29.74	13.07 to 31.73
LOGEC50	1.354 to 1.550	1.325 to 1.620
HILLSLOPE	-2.668 to -1.275	-2.370 to -0.8835
EC50	22.59 to 35.51	21.12 to 41.71
Goodness of Fit		
Degrees of Freedom	7	7
R squared	0.9931	0.9858
Absolute Sum of Squares	48.60	88.53
Sy.x	2.635	3.556
Data		
Number of X values	10	10
# of Y replicates (mean analyzed)	3	3
Total number of values	10	10
Number of missing values	20	20

Figure 25